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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,710	05/08/2002	Audrey Goddard	P3230R1C001-168	8520

30313 7590 07/28/2005

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EXAMINER	
KAUFMAN, CLAIRE M	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,710	GODDARD ET AL.	
	Examiner	Art Unit	
	Claire M. Kaufman	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-6,11-14 and 16-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-6,11-14 and 16-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/9/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.0-0

DETAILED ACTION

Inventorship

In view of the papers filed 5/94/05, the inventorship in this nonprovisional application has been changed by the deletion of D.L. Eaton, E. Filvaroff, M.E. Gerritsen and C. K. Watanabe.

The application will be forwarded for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Response to Arguments

The rejection of claims under 35 USC 101 is withdrawn upon further reconsideration for claims 4-6. However, the claims remain rejected over 35 USC 112, first paragraph, for lacking enablement, and claims 11-14 remain and new claims 16-31 are rejected under 35 USC 101.

The rejections of claims 1-3, 7-10 and 15 are moot in view of the cancellation of the claim.

The rejection of claims 4 and 5 under 35 USC 112, first paragraph, written description, is withdrawn in view of the amendments to the claims. Note that claims 14 and 16-20 remain and new claims 21-31 are, however, rejected.

The rejection of claims under 35 USC 102(b) as anticipated by the GenBank reference is withdrawn in view of arguments concerning the "Stempel Doctrin". That is, because the prior art relied upon teaches no more than Applicants' earliest priority application which discloses SEQ ID NO:75 and 76, Applicants are entitled to a priority date of 9/10/98 (60/099,755). However, a new rejection appears below.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 101/112, First Paragraph

Claims 14-20 remain and new claims 21-31 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth in the previous Office action.

Claims 4-6, 11-14, 16-20 remain and new claims 21-31 are rejected over 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons set forth in the previous Office action, including those which address the new and amended claims:

New claims 21-25 limit the minimum size of the polynucleotide of claim 14. New claims 26-31 are drawn to a nucleic acid at least 95% identical to SEQ ID NO:75 or the coding region thereof. These new claims have the same structural identity requirements as, for example, claim 4, with the exception that they lack a functional limitation. That is, they do not have a limitation giving them utility as a cancer diagnostic tool. Therefore, they do not have utility and are not enabled for the reasons of record and as discussed below and in the previous Office aciton. The amendments to independent claims 4-5 provide limitations which make the claims more structurally narrow than before, but do not overcome the lack of enablement of the claims for reasons of record. These amendments also introduce the problem of how to make nucleic acids which are not identical to SEQ ID NO:75 but are more highly expressed in esophageal tumors compared to normal esophageal tissue.

Applicants' response to the rejection under 35 USC 101 is partly applicable to and support the request for withdrawl of the rejection under 35 USC 112, first paragraph (see Applicants' response on p. 31). As a result, both utility and enablement arguments will be discussed here.

First, it must be stated that the asserted utility for the nucleic acid as a tumor marker for esophageal tumor is accepted. However, the use is not enabled as will be discussed here and the majority of pending claims do not require the that claimed polynucleotide have this utility. Note that polynucleotides identical to SEQ ID NO:75 inherently have this utility. Also, those arguments relating to the enablement of the expressed encoded polypeptide are moot because the claims no longer refer to the polypeptide in this application (see also p. 22, last paragraph, of Applicants' response).

Applicants argue (p. 13 and paragraph bridging pages 21-22) that the phrase "immediate benefit to the public" does not necessarily have to mean the invention is "currently available" to the public in order to satisfy utility requirements. "Rather, *any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient*, at least with regard to defining 'substantial' utility." (MPEP § 2170.01). The argument has been fully considered, but is not persuasive. That section of the MPEP also states that when "further research is required to reasonably confirm the asserted utility, the claims do not meet the requirements of 35 USC 101." The specification has failings which the Examiner pointed out. While current availability of a claimed invention is not always necessary, the invention must still meet the requirements of 35 USC 112, first paragraph. 35 USC 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same ...." For the reasons discussed here and in the previous Office action, it is maintained the specification does not contain an enabling disclosure, and the evidence submitted (including copies of declarations filed in copending cases) does not overcome the insufficiencies of the disclosure. If the claimed polynucleotide is not more highly expressed in esophageal tumor, one cannot use it. While other asserted utilities were discussed in previous Office action such as drug screening and microarray analysis, these utilities are not substantial for the reasons previous stated.

Applicants argue on pages 14-16 that *In re Brana* states that "Usefulness in patent law... necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to administer to humans." The argument has been fully considered, but is not persuasive. While *Brana* did deal with a rejection under 35 USC 112, first paragraph, the rejection was directed toward utility—specific, substantial and credible use—instead of enablement. While it is true that administration of a pharmaceutical to a human is not always necessary for either utility or enablement, one must know how to use the invention without undue experimentation. In the instant situation, Applicants claim a nucleic acid which is at least 95% identical to SEQ ID NO:75 or the coding

region (ORF) thereof or hybridizes under recited conditions to SEQ ID NO:75 and is at least (about) 20 nucleotides in length, which it is maintained the disclosure does not support the use of.

Evaluation of the invention in light of factors to be considered for enablement as set forth in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) is helpful in showing why the instant invention is not enabled. As to the nature of the invention, it is a nucleic acid with no known specific association other than that asserted by Applicants of overexpression in esophageal tumors. It does not encode a protein with a recognized/characterized physiological/biochemical property; although, US 5, 945,511 cited on page 12 of this Office action (US 5,945,511) teaches a polypeptide, highly related to the polypeptide encoded by SEQ ID NO:75 of this application, that is identified only as a class II cytokine receptor. However, nothing about which cytokines activate it or what physiological response it elicits has been disclosed. Therefore, this prior art does not help elucidate an enabling (or specific and substantial) use for PRO1315. The non-identical nucleic acids (those which hybridize or are not 100% identical to SEQ ID NO:75 or its ORF) have not been shown to be overexpressed in any tumors or exist in nature. As to the state of the prior art, other nucleic acids usable for tumor markers had been identified, though none identified as such were identical or highly similar to SEQ ID NO:75. Therefore, the connection of SEQ ID NO:75 to tumors was not known at the time the instant application was filed. While the skill in the art for differential screening has existed for over a decade, interpretation of the results depends, for example, on relative or absolute levels of the difference(s), the ability to generalize to more than one cell culture or tumor type or, conversely, the ability to pinpoint a particular tumor type (*e.g.*, adenocarcinoma *versus* squamal), and repeatability of the differential expression both in terms of frequency/prevalence and quantity/sensitivity. Further, it was not routine to use as a tumor probe a nucleic acid less than 100% identical to the target nucleic acid. There are no working examples of nucleic acids at least 95% identical to or hybridizing under the recited conditions which are overexpressed in esophageal tumors other than SEQ ID NO:75 itself. The breadth of the claims is broad, encompassing structural variation and, in the case of claims 14, 16 and 19-31, no functional limitation. There is very little guidance or direction about using the claimed nucleic acid of SEQ ID NO:75 except the information that it is overexpressed in esophageal

tumors. As discussed in previous Office actions, the specific type of tumor is not disclosed, nor are levels of expression, relative amounts or how many different tumor cDNA libraries from each tumor tissue were screened, for example. For all these reasons and those previous stated, it would require undue experimentation to use the invention as claimed.

On page 16, Applicants cite *Fujikawa v. Wattanasin*, arguing that *in vitro* testing of a pharmaceutical was sufficient to support use *in vivo*. Evidence only needs to be such that the skilled artisan would be convinced of a reasonably probability of the asserted use. The argument has been fully considered, but is not persuasive. At issue is **not** whether *in vitro* microarray/expression data can *per se* support use of differential expression for diagnostic purposes. The issue in this application is the insufficiency of disclosure to allow the skilled artisan to use the claimed invention without undue experimentation. Because as previously discussed there is critical information lacking which includes: whether differences in expression between tumor and normal tissue of SEQ ID NO:75 were significant, over what conditions differences could be detected, and what levels (relative or absolute) were detected in tumor and normal control, the skilled artisan cannot use (whether *in vivo* or *in vitro*) the claimed invention if it is not more highly expressed in esophageal tumor than normal esophageal tissue.

Applicants argue (pp. 19 and 22-23) that the Declaration of Grimaldi (submitted as evidence from a copending application but not filed in the instant application) demonstrates at least a two-fold difference in expression between normal and tumor tissues and the usefulness of the claimed nucleic acid as a diagnostic tool for determining the presence or absence of a tumor. The argument has been fully considered, but is not persuasive. This conclusory statement does not enable the invention because it does not fill important gaps in the disclosure needed to enable using the invention without significant further experimentation, such as expression level range for normal and tumor tissues, specific types of esophageal tumors detectable, and probability of detection for any particular esophageal tumor type (*e.g.*, whether one would reasonably expect overexpression in 10/10 or 1/20 tumors tested). Even though the detection in Example 18 of the specification was carried out using cDNA libraries from tumor and normal tissue sample and, according to the declaration, the libraries were made from pooled samples of tissues, this does not fill the above discussed gaps. It is noted that Grimaldi in paragraph 6 of the declaration describes the detection as "semi-quantitative" and the specification for Example 18 as "standard

quantitative". The declaration also says (¶5) that "Data from a pooled sample are more likely to be accurate than data from a single individual." This begs the question of whether the tissue from an individual could be assessed for whether or not it is cancerous. Clinical diagnostics are not usually geared toward a populous but toward an individual's particular condition. While a "relative difference in expression between normal tissue and suspected cancerous tissue" can be informative, without more specifics about necessary sample size, expression level range for normal and tumor tissues, types of esophageal tissue that can used, and other questions, the specification has not provided the invention in an enabling form. Therefore, even accepting Dr. Grimaldi's opinion, the declaration is insufficient to overcome the rejection of the claims under 35 USC 101 and 112, first paragraph, for the reasons discussed above.

Applicants argue in the paragraph bridging pages 19-20 that the utility of gene product does not have to depend on the function of the encoded gene product and that polymorphisms which may not cause a disease have been allowed to be patented. The argument has been fully considered, but is not persuasive. In the instant case, the encoded gene product does not have utility. Also, in the instant situation, if the claimed polynucleotide cannot be used as a diagnostic tool for esophageal tumors, it does not have utility as discussed here and in the previous Office action. Finally, each application is examined on its own merits.

Applicants argue (pages 20-21) that the results of Hu et al. (J. Proteome Res., 2003, previously cited) are not surprising and provide little if any information about genes with less than 5-fold differential expression tumor compared to normal tissue. The argument has been fully considered, but is not persuasive. While there are shortcomings of the technique used by Hu et al., the findings are suggestive of a correlation between expression level and activity. The caution provided in the last paragraph of p. 411 is noteworthy: "It is not uncommon to see expression changes in microarray experiments as small as 2-fold reported in the literature. Even when these expression changes are statistically significant, it is not always clear if they are biologically meaningful." As discussed above, it is not clear that the expression changes listed in Example 18 of the instant specification are significant.

Applicants argue (pages 27-28) that it is more likely than not that the gene encoding the POR1315 polypeptide is more highly expressed in esophageal tumor tissue than normal tissue. While this statement is correct, the claims are not drawn that narrowly and the specification is

deficient in information, examples or guidance that would allow the skilled artisan to use the broadly claimed polynucleotides without undue experimentation as discussed here and in the previous Office action.

Applicants argue (p. 29) that the role of a gene in a cancer is not necessary to enable its use as a diagnostic tool for tumor detection. The argument has been fully considered, but is not persuasive. It is correct that the role of a gene need not be known, but the specification and/or prior art needs to enabled that particular gene to be used diagnostically. In this case, the prior art provides no information about the use of the gene as it relates to cancer, and the specification does not provide an enabling disclosure for use of the PRO1315 nucleic acid as a diagnostic tool for esophageal tumors based on differential expression for the reasons discussed above and in previous Office actions. As to the claims drawn to nucleic acids not identical to SEQ ID NO:75 or its ORF, even if SEQ ID NO:75 were enabled for a diagnostic tool, nucleic acids not identical would not be because it was not routine or expected for the skilled artisan to use a probe not identical to the target nucleic acid sequence for detection of the target nucleic acid when the sequence of the target nucleic acid was known. Also, with unknown relative differences, it is unpredictable how different a polynucleotide probe could be from SEQ ID NO:75 and be used for detecting differential expression.

Applicants argue (p. 31) that one skilled in the art would know how to make the claimed nucleic acids. The argument has been fully considered, but is not persuasive. While one could make a nucleic acid which is 95-99% identical to or which hybridizes to SEQ ID NO:75, it would require undue experimentation to make a nucleic which is both 95-99% identical to or which hybridizes to SEQ ID NO:75 and which is more highly expressed in esophageal tumors compared to normal esophageal tissue, respectively. For claims 4 and 5 (and dependent claims 17-20), the nucleic acids need to have not only a particular structural relationship to SEQ ID NO:75, but must also naturally occur in esophageal tumors. The specification has not taught any nucleic acid except SEQ ID NO:75 expressed in those tumors. There is no direction or guidance about predicting what other structurally related nucleic acids would have the necessary expression, nor does the prior art provide information to aid the skilled artisan in this determination.

On the same page, Applicants argue that one could use nucleic acids which are both 95-99% identical to or which hybridizes to SEQ ID NO:75 and which are more highly expressed in esophageal tumors compared to normal esophageal tissue. The argument has been fully considered, but is not persuasive. For the reasons discussed in the previous Office action and above, neither the nucleic acid of SEQ ID NO:75 nor those less identical are enabled for use as a diagnostic tool of esophageal tumors. Further, for claims 14, 16 and 21-31, which are drawn to nucleic acids not identical to SEQ ID NO:75 and which have no functional limitation, one skilled in the art would not know how to use these for the reasons previously discussed.

Claim Rejections - 35 USC § 112

Claims 14, and 16-20 remain and new claims 21-31 are rejected over 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons set forth in the previous Office action.

Applicants argue (p. 33-35) that if there are sufficient identifying characteristics, *e.g.*, functional characteristic coupled to a structure, there is sufficient written description. In the instant application the function is expression of the nucleic acid in normal esophagus and relatively higher expression in esophageal tumor. The argument has been fully considered, but is not persuasive. The point is that **not** all polynucleotides 95% or 99% identical to SEQ ID NO:75 are included. Not all the claims require particular tissue expression. Only those nucleic acids that naturally occur in esophagus are included for claims 4 and 5. Applicants have disclosed no concept of which nucleic acid(s) which is not identical to SEQ ID NO:75 is present in esophagus. The specification does not convey to one of skill in the art, including recombinant DNA/protein technology art, that the inventors were in possession of these non-identical naturally occurring claimed proteins. The specification does not provide information so the skilled artisan could readily envision such nucleic acids. Contrary to Applicants assertion (p. 35), this situation is like *Fiddes v. Baird* because the structure of other nucleic acids with the

same expression pattern and the required structural limitation cannot be conceived based on the single species disclosed.

Applicants additionally argue at pages 33-34 that there is sufficient written description for those claimed nucleic acids not identical to SEQ ID NO:75 with no functional limitation specified, and that the finding in the *Enzo* case support the claimed invention having adequate written description. This argument has been fully considered but is not deemed persuasive because (a) the fact situation in the *Enzo* case is substantively different from that in the instant case. The *Enzo* claims are drawn to a "composition of matter that is specific for *Neisseria gonorrhoeae*", which is then further described by ATCC deposit number and sequences that hybridize to such. It is further noted that the hybridization recitation in *Enzo* is substantively different than that herein, as it requires a comparative hybridization that demonstrates specificity of the claimed composition for one strain of *Neisseria* over another. By contrast, the instant claims have *no* functional limitations. Similarly, Example 9 of the Written Description Guidelines Training Materials is not applicable here, as the fact situation described therein is:

> The specification discloses a single cDNA (SEQ ID NO:1) which encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity. The specification includes an example wherein the complement of SEQ ID NO: 1 was used under highly stringent hybridization conditions (6XSSC and 65 degrees Celsius) for the isolation of nucleic acids that encode proteins that bind to dopamine receptor and stimulate adenylate cyclase activity. The hybridizing nucleic acids were not sequenced. They were expressed and several were shown to encode proteins that bind to a dopamine receptor and stimulate adenylate cyclase activity. These sequences may or may not be the same as SEQ ID NO: 1.

The nucleic acids claimed herein are not required to encode a protein, much less one with adenylate cyclase or other well-characterized activity. Similarly, Example 14 is drawn to a protein with a well defined function, and a claim that is limited to 95% identity to the claimed sequence and has a functional limitation and is not required to be naturally occurring. The fact situation therein is substantively different from that of the instant application. For these reasons and those previously of record, the rejection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14, 16, 21-25 and dependent claims 17-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Amended and new claims 14, 16 and 21-25 are indefinite for reciting "at least about" X nucleotides in length. It is unclear what range is intended by "at least about". At least 10 nucleotides means 10 or more. It is not clear if "at least about" means, for example, at least 10 or can be less than (about) 10.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 4 and 12-17are rejected under 35 U.S.C. 102(e) as being anticipated by US 5,945,511.

US 5,945,511 teaches a Zcytor7 polynucleotide (SEQ ID NO:1) which is at least 99% identical to the region encoding the extracellular domain of SEQ ID NO:76 and to SEQ ID NO:76 minus its signal sequence (see sequence comparison for AF184971 to SEQ ID NO:75 and 76 presented on the last pages of the previous Office action). SEQ ID NO:1 is also at least 95% identical to full-length coding region of SEQ ID NO:75 of the instant application.

For amended claims 4-5, which require higher expression in esophageal tumor compared to normal esophageal tissue, because the nucleic acid of SEQ ID NO:75 of the instant

application is identical except for a single mismatch to the ORF of SEQ ID NO:1 for the mature protein of US 5,945,511, one would reasonably expect the two naturally occurring nucleic acids to have the same tissue expression pattern. The prior art nucleic acid meets the structural limitations of the new claims of the instant application.

Applicants argue that the instant application receives an effective filing date of 08/10/98. In view of the new rejection above, US 5,945,511 is prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (571) 272-0873. Dr. Kaufman can generally be reached Monday, Tuesday and Thursday from 9:00AM to 3:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (571) 272-0829.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Official papers filed by fax should be directed to (571) 273-8300. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Claire M. Kaufman, Ph.D.

Patent Examiner, Art Unit 1646

June 23, 2005

Docket No

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are **as stated** below next to my name;

I believe I am the original first and sole inventor (if only one name is listed below) or an original, first and joint inv names are listed below) of the subject matter which is claimed and for which a patent is sought on the inventi

SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE S

the specification of which (check one) X is attached hereto or was filed on as Application Serial No. and was ar applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordanc Code of Federal Regulations, Section 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119(a)-(d) of any foreign application(s inventor's certificate listed below and have also identified below any foreign application for patent or inventor's cer filing date before that of the application on which priority is claimed:

Prior Foreign Application(s): Prior Yes

Number	Country	Day/Month/Year Filed

I hereby claim the benefit under Title 35, United States Code, §119(e) of any United States provisional applications(s

Please see attached Appendix A (Listing 87 U.S. Provisional Patent Applications)

Application Ser. No. Filing Date

I hereby claim the benefit under Title 35, United States Code, §120 of any United States applications(s) listed belo as the subject matter of each of the claims of this application is not disclosed in the prior United States application provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material i defined in Title 37, Code of Federal Regulations, §1.56 which occurred between the filing date of the prior applic national or PCT international filing date of this application:

Please see attached Appendix B (Listing 20 U.S. applications and 27 PCT applications

Application Ser. No. Filing Date Status: Patented, Pending, Abandon

Application Ser. No. Filing Date Status: Patented, Pending, Abandon

POWER OF ATTORNEY: As a named inventor, I hereby appoint all Attorney(s) and/or Agent(s) associated with Patent Office Issued Customer Number to prosecute this application and transact all business in the Patent and Tra connected therewith.

09157

PATENT TRADEMARK OFFICE

Paul E. Rauch, Registration No. 38,591, CUSTOMER NUMBER: 28,442

dlc 7/20/05 See paper filed 5/9/05 for inventorship change